

(b) a polypeptide comprising a portion of the amino acid sequence set forth in SEQ ID NO: 6 effective to cleave APP, wherein the polypeptide lacks amino acids 1-45 of SEQ ID NO: 6.

167. A purified polynucleotide comprising a nucleotide sequence that encodes a polypeptide of claim 151.

168. A polynucleotide according to claim 167, selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO: 3;
- (b) a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO: 5;
- (c) a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO: 7;
- (d) a polynucleotide comprising a nucleotide sequence that is at least 95% identical to (a), (b), or (c), and that encodes a polypeptide that cleaves APP; and
- (e) a fragment of (a), (b), (c), or (d) that encodes a polypeptide that cleaves APP.

169. A polynucleotide according to claim 167 comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS: 21, 23, 25, 27, 29, and 31.

170. A purified polynucleotide according to claim 167, selected from the group consisting of:

- (a) a purified polynucleotide that comprises a nucleotide sequence that encodes amino acids 22-501 of SEQ ID NO: 4 and lacks adjacent nucleotide sequence encoding amino acids 1-21 of SEQ ID NO: 4; and
- (b) a purified polynucleotide that comprises a nucleotide sequence that encodes amino acids 22-476 of SEQ ID NO: 6 and lacks adjacent nucleotide sequence encoding amino acids 1-21 of SEQ ID NO: 6.

171. A purified polynucleotide according to claim 167, selected from the group consisting of:

(a) a purified polynucleotide comprising a nucleotide sequence that encodes a portion of the human Asp2(a) amino acid sequence set forth in SEQ ID NO: 4 effective to cleave APP, and wherein the polynucleotide lacks adjacent nucleotide sequence encoding transmembrane domain amino acid residues 455-477 of SEQ ID NO: 4; and

(b) a purified polynucleotide comprising a nucleotide sequence that encodes a portion of the human Asp2(a) amino acid sequence set forth in SEQ ID NO: 6 effective to cleave APP, and wherein the polynucleotide lacks adjacent nucleotide sequence encoding transmembrane domain amino acid residues 430-452 of SEQ ID NO: 6.

172. A purified polynucleotide according to claim 171, said polynucleotide lacking nucleotide sequence encoding amino acids 454-501 of SEQ ID NO: 4.

173. A purified polynucleotide according to claim 167 comprising a fragment of a mammalian Asp2 polynucleotide, wherein the fragment lacks nucleotide sequence encoding the transmembrane domain of said mammalian Asp2 polypeptide.

174. A purified polynucleotide according to claim 167, wherein the polynucleotide lacks a nucleotide sequence encoding a mammalian Asp2 pro-peptide sequence.

175. A vector comprising a polynucleotide according to claim 167.

176. A vector according to claim 175 that is an expression vector wherein the polynucleotide is operably linked to an expression control sequence.

177. A host cell transformed or transfected with a polynucleotide according to claim 167.

178. A host cell transformed or transfected with a vector according to claim 176.

179. A host cell according to claim 178 that is a mammalian cell.

180. A host cell according to claim 178 that expresses the polypeptide on its surface.

181. A host cell according to claim 178 that secretes the polypeptide encoded by the polynucleotide, wherein the secreted polypeptide lacks a transmembrane domain.

182. A host cell according to claim 177, wherein the host cell is transfected with a nucleic acid comprising a nucleotide sequence that encodes an amyloid precursor protein (APP) or fragment thereof that includes a protease recognition site recognized by the polypeptide.

183. A host cell according to claim 182, wherein the host cell is transfected with a nucleic acid comprising a nucleotide sequence that encodes an amyloid precursor protein (APP).

184. A host cell according to claim 183, wherein the host cell is transfected with a nucleic acid comprising a nucleotide sequence that encodes an amyloid precursor protein (APP) that includes two carboxy-terminal lysine residues.

185. A host cell according to claim 182, wherein the APP or fragment thereof includes the APP Swedish mutation sequence KM → NL immediately upstream of the  $\beta$ -secretase cleavage site.

186. A host cell according to claim 182 that expresses the polypeptide and the APP or APP fragment on its surface.

187. A method of making a polypeptide that cleaves APP, comprising steps of culturing a host cell according to claim 177 in a culture medium under conditions in which the cell produces the polypeptide that is encoded by the polynucleotide.